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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/572,175	05/16/2007	Stefan Golz	Le A 36 839	7833

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EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,175	GOLZ ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2009*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-23* is/are pending in the application.

4a) Of the above claim(s) *2,3,11-13 and 16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9,14,15 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office Action is in response to the paper filed August 24, 2009.

Claim 10 has been canceled. Claims 1-9 and 11-23 are currently pending. The Examiner has withdrawn Claims 2, 3, 11-13, and 16-19 from further consideration because these claims are drawn to non-elected inventions. Claims 1, 4-9, 14, 15, 20, and 21-23 are currently under examination.

Benefit of priority is set to September 16, 2003.

Withdrawal of Rejections:

The rejection of Claims 14, 15, 20, and 21 under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, is withdrawn.

Maintenance of Rejections:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-9, 14, 15, 20, and 21 new Claims 22 and 23 are again rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 1, stringent conditions are not set forth in the claims or defined in the specification. Therefore, this term cannot be understood by the skilled artisan.

In Claim 1, it is not understood what is intended by the limitation that the nucleic acid differs from a nucleic acid that hybridizes to SEQ ID NO: 1 by the degeneracy of the genetic code, that is, this claim limitation appears to be a reach through limitation because one cannot know what the degenerate code of an unknown nucleic may be.

In Claim 1, the term "homology" is used. This term is a qualitative term and not a quantitative term; therefore, one skilled in the art cannot know what 95% or 65% homology means.

Applicants urge at page at page 8 that the specification defines stringent conditions. The Examiner notes that the stringent hybridization conditions are exemplary and not limiting. Therefore, this aspect of the rejection is maintained.

Applicants urge at page 9 that because the stringency conditions are set forth in the specification, one skilled in the art would know the degenerate code of a nucleic acid that hybridized to nucleic acid encoding SEQ ID NO: 2. The Examiner again points out that the stringent hybridization conditions are exemplary and not limiting. Therefore, this aspect of the rejection is maintained.

Applicants urge that the term homology is definite because they have cited the Blast method. Homology is the qualitative relatedness of nucleic acids and proteins. Sequence identity is quantitative and is a measure of the number of nucleotides or amino acids that are shared between two nucleic acid or amino acid sequences. For example, steroid hormone receptors have a pattern of cysteines in which the cysteines are separated by invariant numbers of amino acids. Thus, steroid hormone receptors

have high homology based on their cysteine motif, and are identified accordingly (orphan receptors), but have low sequence identity. The proper term when referring to a per cent shared nucleotides or amino acids between two nucleic acids or two amino acids is “identity”.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-9, 20, and 21 are again rejected under 35 U.S.C. 102(b) as being anticipated by Inouye et al. (1993; Cloning and sequence analysis of cDNA for the Ca2+-activated photoprotein, clytin. FEBS 315(3): 343-346).

Inouye et al. teach nucleic acid encoding clytin, this nucleic acid sharing 50.9% identity with SEQ ID NO: 1 and encoding clytin sharing 77.5% identity with SEQ ID NO: 2. The nucleic acid comprises at least 10 consecutive nucleotides from SEQ ID NO: 1, for example, nucleotides 105-147 of the nucleic acid taught in Inouye et al. are the same as nucleotides 221-263 of instant SEQ ID NO: 1. The nucleic acid encoding clytin was placed into vector pBluescript (page 344. left col, last line), the vector was transformed into E. coli (page 344. left col, last line), and expressed and purified therefrom (page 344, right col., line 9).

Therefore, Inouye et al. teach a nucleic acid whose complementary strand would be expected to hybridize with SEQ ID NO: 1 and encoding a photoprotein because the

nucleic acids share high sequence identity and clytin is a photoprotein (**Claim 1c, d**). **Claim 1e and 1f** are included in this rejection because one cannot know which parts are considered to be homologous, such that they are 95% or 65% homologous to SEQ ID NO: 1 – see the rejection under 112/2 above. The nucleic acid encoding clytin is an oligonucleodie comprising at least 10 consecutive nucleotides of SEQ ID NO: 1 (**Claim 7**). Inouye et al. teach placing the nucleic acid into a vector (**Claim 5**) and therefore having a 5' functional promoter (**Claim 4**). The vector was placed into E. coli, an organism (**Claim 6**), and the polypeptide was expressed therefrom (**Claim 9**); therefore, the nucleic acid was used as a marker or reporter gene (**Claim 21**) and the protein a label or reporter (**Claim 20**). Clytin is the protein encoding by the nucleic acid taught in Inouye et al. (**Claim 8**).

Applicants urge that Inouye et al. do not disclose a nucleic acid molecule having at least 65% homology to SEQ ID NO: 1. See the Examiner's explanation of homology above.

New Rejections:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 8, 20, 22, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Stults et al. (1997; USP 5,648,218) as evidenced by Inouye et al. (1993; Cloning and sequence analysis of cDNA for the Ca2+-activated photoprotein, clytin. FEBS 315(3): 343-346).

Stults et al. claim:

1. **A photoprotein-binding reagent conjugate** composition comprising a sulfhydryl-activated photoprotein coupled to a maleimide activated binding reagent, said conjugate composition capable of emitting light.

2. The composition of claim 1, wherein said sulfhydryl-activated photoprotein is modified to contain at least one sulfhydryl group more than is present in an unmodified photoprotein, and wherein said maleimide activated binding reagent is modified so as to crosslink with at least one sulfhydryl group on said photoprotein.

3. The composition of claim 1 wherein said **photoprotein is** selected from the group consisting of apoaequorin, aequorin, apo-obelin, obelin, apo-mnemiopsin, mnemiopsin, apo-berovin, berovin, pholasin, **clytin**, halistovein thalassiciolin and bioluminescent proteins isolated from Pelagia, or ostracods.

4. The composition of claim 1 wherein said **binding reagent** is selected from the group consisting of streptavidin/avidin, lectins, **enzymes**, glycoproteins, peptides, hormones, **receptors**, antigens, **drugs**, **antibodies** and antigen binding fragments of said antibodies thereof, and RNA and DNA oligonucleotides.

As set forth above, Inouye et al. teach nucleic acid encoding clytin, this nucleic acid sharing 50.9% identity with SEQ ID NO: 1 and encoding clytin sharing 77.5% identity with SEQ ID NO: 2. The nucleic acid comprises at least 10 consecutive

nucleotides from SEQ ID NO: 1, for example, nucleotides 105-147 of the nucleic acid taught in Inouye et al. are the same as nucleotides 221-263 of instant SEQ ID NO: 1.

Therefore, Stults et al. teach a photoprotein clytin encoded by the nucleic acid set forth in instant Claim 1 (**Claim 8, 20**), wherein the clytin is coupled to an additional protein (**Claim 22),** wherein the additional protein is an antibiotic (drug), enzyme, receptor, or antibody (**Claim 23**).

Claims 1, 4-9, 14, 15, 20, 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Foti et al. (priority to October 21, 2002; USP 7,601,805) as evidenced by Inouye et al. (1993; Cloning and sequence analysis of cDNA for the Ca2+-activated photoprotein, clytin. FEBS 315(3): 343-346).

Foti et al. teach Photin, a chimeric photoprotein wherein amino acids 50-94 of obelin is replaced with amino acids 53-97 of clytin (Col. 3, lines 9-15). The cDNA encoding Photin is taught in Example 1, in vitro translation in Example 2, CHO expression of Photin in Example 3 at Col. 7 at 3.2 and 3.3, the cDNA encoding Photin was placed into the pcDNA3 vector under the T7 promoter (Col. 8, lines 28-32).

As set forth above, Inouye et al. teach nucleic acid encoding clytin, this nucleic acid sharing 50.9% identity with SEQ ID NO: 1 and encoding clytin sharing 77.5% identity with SEQ ID NO: 2. The nucleic acid comprises at least 10 consecutive nucleotides from SEQ ID NO: 1, for example, nucleotides 105-147 of the nucleic acid taught in Inouye et al. are the same as nucleotides 221-263 of instant SEQ ID NO: 1.

Therefore, Foti et al. teach an isolated nucleic acid encoding clytin as evidenced by Inouye et al. to meet the limitations of **Claim 1, 7 and 21**, the nucleic acid operatively linked to the functional promoter T7 (**Claim 4**) and placed into the pcDNA3 vector (**Claim 5**) and transformed into a CHO cell (**Claim 6**) to produced clytin (**Claim 9**), the nucleic acid comprising a nucleic acid encoding clytin and another nucleic acid not encoding clytin, which in the case of photin is obelin (**Claim 14**).

Therefore, Foti et al. teach an isolated polypeptide clytin as evidenced by Inouye to meet the limitations of **Claim 8 and 20**, wherein the photin protein is a fusion protein comprising obelin and clytin (**Claim 15).**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson whose telephone number is 571-272-0946. The examiner can normally be reached on 6:00 AM - 4:00 PM, Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen Cochrane Carlson/
Primary Examiner, Art Unit 1656